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Intensive care unit and hospital mortality in patients with obstructive sleep apnea☆,☆☆

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ABSTRACT

Introduction: Obstructive sleep apnea (OSA) is a common disorder affecting between 5% and 24% of men and women. The prevalence of OSA in the intensive care unit (ICU) population is unknown. This study was undertaken to determine the prevalence of OSA in patients admitted to the ICU and to determine if OSA is an independent predictor of mortality.

Methods: This is a retrospective study using an Acute Physiology and Chronic Health Evaluation III database cross-referenced to a comprehensive clinical database to identify patients with and without OSA admitted to medical, surgical, and mixed ICUs at a large academic medical center.

Results: Between January 2003 and December 2005, 15 077 patients were admitted to the ICUs; and of these, 1183 (7.8%) had a physician-documented diagnosis of OSA. Eight hundred thirty-five (71%) patients had polysomnographic testing at our institution with a documented apnea-hypopnea index more than 5 per hour. Patients with OSA were younger (59.1 ± 14.0 vs 62.3 ± 18.0), male (58.9% vs 53.7%), and had lower Acute Physiology and Chronic Health Evaluation III scores (45.3 ± 24.1 vs 54.9 ± 27.7). Predicted mortality (10.3% ± 16.4% vs16.3 ± 21.7), median ICU length of stay (1.13 vs 1.50 days), ICU mortality (2.4% vs 6.2%), and hospital mortality (3.9% vs 11.4%) were all reduced in patients with OSA, *P* values < .001. When adjusted for the severity of illness, OSA was independently associated with decreased hospital mortality, (0.408; 95% confidence interval, 0.298-0.557).

Conclusions: Obstructive sleep apnea is common in patients admitted to the ICU. Obstructive sleep apnea was associated with a reduction in both ICU and hospital mortality.

1. Introduction

Obstructive sleep apnea (OSA) is a common medical condition affecting 5% to 25% of men and women worldwide [1-3]. Obstructive sleep apnea is characterized by a reduction or cessation in airflow during sleep due to recurrent occlusions of the pharynx despite ongoing inspiratory effort. This results in oxyhemoglobin desaturation and arousals from sleep leading to sleep fragmentation and daytime symptoms. Obstructive sleep apnea hypopnea syndrome is defined by apneas, hypopneas, and respiratory effort related arousals, of greater than 5 per hour of sleep in a symptomatic patient (eg, excessive daytime sleepiness, fatigue, mood disturbances, and concentration difficulties). Obstructive sleep apnea has recently emerged as an important independent risk factor for cardiovascular disease [4,5].

Patients with OSA have a high incidence of comorbid conditions commonly present in patients admitted to the intensive care units (ICU), including obesity, diabetes mellitus, hypertension, ischemic heart disease, heart failure, and cerebrovascular disease [6]. Sleep disordered breathing has also been identified as a common contributing cause of hypercapneic respiratory failure in obese patients admitted to the ICU [7]. Because of these associations, it has been assumed that OSA patients have increased morbidity and mortality when admitted to an ICU. A recent study found that OSA patients were more likely to require ICU transfer and intubation or noninvasive positive pressure ventilation after surgery [8]. The prevalence of OSA, however, in the ICU population is unknown. It is also unknown whether OSA is an independent risk factor for mortality or morbidity in the ICU or hospital setting. This study was undertaken to determine the prevalence of OSA in patients

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admitted to medical, surgical, and mixed ICUs at a large academic medical center and to determine if OSA is an independent predictor of ICU and hospital mortality.

2. Material and methods

This study included all patients who were admitted to 3 ICUs (medical, surgical, and mixed) at Mayo Clinic between January 2003 and December 2005. Study was approved by the Mayo Clinic Institutional Review Board. The study did not require a separate ethics committee approval. Patients were identified using the Acute Physiology and Chronic Health Evaluation (APACHE) III database, which included all patients admitted to our ICUs during this period. Patients aged younger than 16 years and those who stayed in the ICU less than 4 hours are not included in the APACHE III database. Patients who did not authorize review of their medical records for research activities were excluded. Study patients were then cross-referenced to a comprehensive clinical database to identify patients with a diagnosis of OSA. The clinical database includes all physician-documented diagnoses for patients seen at our institution using Hospital International Classification of Disease Adaptation (HICDA) codes, a modified version of *International Classification of Diseases*, *Eighth Revision* codes [9]. A computer-generated search using medical index HICDA codes was performed to identify all patients with a recorded diagnosis OSA or sleep apnea from January 1977 to December 2006. Patients with HICDA codes corresponding to central sleep apnea or Cheyne-Stokes respiration were excluded. Patients were then cross-referenced to a comprehensive polysomnography (PSG) database encompassing all patients who have undergone PSG testing at Mayo Clinic between January 1988 and December 2006. The apnea-hypopnea index or equivalent (eg, disordered breathing index) was extracted for patients with OSA.

Illness severity was classified using APACHE III scores available for adult medical and surgical patients from a prospective database that is maintained at Mayo Clinic for quality assurance purposes. This database has previously been used in published reports evaluating ICU outcomes and the performances of various Mayo ICUs. The following variables were abstracted from the APACHE III database: age, sex, comorbidities, source of admission (ward, emergency department, and transfer), ICU admission category (low-risk monitor, high-risk monitor, and active), type of ICU (medical, surgical, and mixed), reason of ICU admission, first ICU day Acute Physiology Score (APS), APACHE III score, and predicted hospital mortality. Intensive care unit length of stay, duration of mechanical ventilation, ICU readmission, and hospital mortality were also extracted. The APACHE related severity scores were calculated as per Knaus et al [10].

3. Statistical analysis

Data were summarized as mean (SD), median (interquartile range), or proportions. Comparisons between groups were made using χ^2 test for categorical variables and either Student *t* tests or Wilcoxon rank sum test for continuous variables. A logistic regression model was created by entering the presence of OSA and first day predicted mortality rate to determine the independent effect of OSA on mortality. When appropriate, odds ratio (OR) and 95% confidence interval (CI) were calculated. *P* values < .05 were considered statistically significant. All analyses were done using SPSS 13.0 (SPSS, Chicago, IL).

4. Results

During the study period, 15 590 admissions to our ICUs were identified. Five hundred thirteen patients were excluded due to absence of prior signed research authorization. Of the 15 077 study patients, 1183 (7.8%) had a physician-documented diagnosis of OSA. Of these, 835 (71%) had a PSG at our institution with a documented apnea-hypopnea index more than 5 per hour or disordered breathing index more than 5 per hour. Mean apnea-hypopnea index was 21 ± 8 per hour.

Table 1
Characteristics of study patients with and without sleep-related disordered breathing

	Sleep disordered breathing, n = 1183	No sleep disordered breathing, n = 13 894	*P*
Age, y, mean (SD)	59.1 (14.0)	62.3 (18.0)	<.001
Male sex (%)	697 (58.9%)	7457 (53.7%)	.006
Ethnicity			.002
American Indian	1 (<1%)	86 (<1%)	
Asian	1 (<1%)	116 (<1%)	
Black	11 (<1%)	181 (1.3%)	
Hispanic	7 (<1%)	117 (<1%)	
Other	38 (3.2%)	625 (4.5%)	
White	1123 (94.9%)	12 732 (91.6%)	
Not available	2 (<1%)	37 (<1%)	
Admission ICU			<.001
Surgical	530 (44.8%)	4995 (36.0%)	
Medical	388 (32.8%)	5095 (36.7%)	
Mixed	265 (22.4%)	3804 (27.4%)	
Admission category			<.001
Low risk	395 (33.4%)	4242 (30.5%)	
High risk	96 (8.1%)	2126 (15.03%)	
Active	692 (58.5%)	7526 (54.2%)	
APS, mean (SD)	35.3 (21.1)	41.8 (24.7)	<.001
APACHE III, mean (SD)	45.3 (24.1)	54.9 (27.7)	.001
Predicted mortality, %, mean (SD)	10.3 (16.4)	16.3 (21.7)	<.001
ICU mortality	28 (2.4%)	863 (6.2%)	<.001
Hospital mortality	46 (3.9%)	1577 (11.4%)	<.001
ICU LOS (median, d)	1.13 (0.83-2.46)	1.50 (0.83-2.976)	

LOS indicates length of stay.

Characteristics and differences between the group of patients with OSA and those without OSA in the study population are presented in Table 1. Patients with OSA were younger (59.1 ± 14.0) compared with the group without OSA (62.3 ± 18.0). Obstructive sleep apnea patients were more likely to be males (58.9% vs 53.7%). There was a large predominance of White patients in both groups, 94.9% in the OSA group and 91.6% in the group without OSA. The group of patients with OSA appeared to be less critically ill, based on lower APACHE III score (45.3 ± 24.1 vs 54.9 ± 27.7), APS (35.3 ± 21.1 vs 41.8 ± 24.7), and lower predicted mortality (10.3% ± 16.4% vs 16.3% ± 21.7%), all with *P* values < .001.

Obstructive sleep apnea patients had significantly lower ICU mortality (2.4% vs 6.2%) as well as hospital mortality (3.9% vs 11.4%). Patients in the OSA group had shorter median ICU length of stay, 1.13 (0.83-2.46) vs 1.50 days (0.83-2.96). After adjusting for the severity of illness as measured by APACHE III–predicted mortality rate, OSA was independently associated with decreased hospital mortality (OR, 0.408; 95% CI, 0.298-0.557, *P* < .001) (Table 2).

5. Discussion

We show that OSA is common in patients admitted to the ICU. The prevalence of OSA in this retrospective study of patients admitted to medical, surgical, and mixed ICUs was 7.8%. Although the prevalence of OSA in the general population has been well studied, this is the first study to document the prevalence of OSA in the ICU patient population. Our study further demonstrates that OSA is associated with a reduction in both ICU and hospital mortality.

Epidemiological studies have shown that OSA is a common disorder affecting men and women worldwide. The prevalence of OSA has been reported to be equivalent to that of diabetes. Obstructive sleep apnea is

Table 2
Multivariate logistic regression analysis

	OR (95% CI)	*P*
Predicted mortality, %	1.042 (1.039-1.044)	<.001
Sleep disordered breathing		
Absent	Reference	–
Present	0.408 (0.298-0.557)	<.001

also emerging as an important independent risk factor for cardiovascular disease [4,11]. Patients with OSA are more likely to be obese and to have comorbid conditions such as diabetes, which are common in the ICU patient population. Despite this, the potential effect of OSA on ICU mortality and overall hospital mortality has not been studied previously. Interestingly in our study, both ICU mortality (2.4% vs 6.2%) and hospital mortality (3.9% vs 11.4%) were significantly lower for patients with a diagnosis of OSA compared with those without OSA. After adjusting for severity of illness based on APACHE III scores, hospital mortality was lower for patients with OSA. The adjusted OR for mortality in the OSA group was 0.408 (95% CI, 0.298-0.557) compared with the group without OSA. These results suggest that OSA is independently associated with reduced hospital mortality. These findings were unexpected.

A potential explanation for the improved outcomes found in patients with OSA may be the protective effects of obesity during critical illness. Obesity is a risk factor for the development of OSA, and large epidemiological studies report that 60% to 90% of patients with OSA are obese. Vgontzas et al reported that 40% of obese men have OSA [12]. The effects of obesity on ICU and hospital mortality have been investigated by several recent studies. Most studies suggest that obesity is independently associated with a better outcome in the ICU. Garrouste-Orgeas et al [13] reported that a body mass index (BMI) more than 30 was protective during critical illness and was associated with favorable outcomes, whereas a low BMI (<18.5) was linked to higher mortality in the ICU. In a large retrospective study, Tremblay and Bandi [14] also found lower ICU mortality rates for overweight and obese patients. Why obesity provides protection during critical illness is unclear. It has been postulated that increased nutritional reserves may play a protective role. The protective effect of obesity during critical illness, however, remains controversial with some studies showing no benefit or increased ICU mortality [15,16]. The different definitions of obesity used in various studies may contribute to these conflicting results.

The diagnosis of OSA requires formal PSG testing. Treatment for OSA includes continuous positive airway pressure (CPAP), upper airway surgery, dental appliances, positional therapy, and weight loss. Continuous positive airway pressure therapy has been shown to improve symptoms as well as having beneficial effects on hypertension [17,18]. The effects of CPAP on mortality in patients with OSA remain controversial; however, a beneficial effect has recently been shown in severe patients [19]. Initiation of CPAP requires an overnight titration PSG. Guidelines recommend routine follow-up after initiation of CPAP therapy. Another possible explanation for our findings is that patients with OSA may be better integrated into the health care system, resulting in closer follow-up and management of associated comorbidities including cardiovascular disease. Once admitted to the ICU, stricter monitoring and a higher level of alertness with regards to detection of respiratory problems may also play a role, making patients with OSA more likely to receive therapies such as noninvasive positive pressure ventilation earlier [8]. The relationship between OSA and cardiovascular risk has been well documented. Studies show a mortality benefit in patients with moderate-to-severe OSA who are compliant with treatment [19]. Although our study did not assess treatment compliance or severity of OSA, this could be another postulated mechanism to help explain our findings.

In our study, OSA patients had lower APS and APACHE III scores and lower predicted mortality. Mean length of stay was also reduced. This suggests that physicians may have a lower threshold to admit patients with OSA to the ICU. A recent study demonstrated higher rates of ICU admission for patients with a diagnosis of OSA after orthopedic surgical procedures [8]. Although our study found that patients in the OSA group were younger than their non-OSA counterparts, this would be an unlikely explanation, as previous studies have found that younger patients have an increased risk of ICU mortality [20]. Although it did not reach statistical significance, there was a trend toward a higher representation of males in the OSA group. This was not unexpected given the higher prevalence of OSA in males [2]. There was also a higher representation of surgical ICU patient in the OSA group.

There are several limitations to our study. It is a single-center retrospective study, and the generalizability of our results is unknown. Body mass index data were not collected; and without this data, we are not able to confirm the hypothesis that the effects of obesity may be contributing to the lower mortality rates found in OSA patients. Lastly, we were not able to differentiate in our database treated vs untreated OSA patients. This issue is being addressed in a follow-up study. There potentially may have been undiagnosed OSA patients in the group without OSA. To reduce the potential effects of this on our analysis, our database search included diagnoses for patients determined up to 1 year after their ICU admission. Despite these limitations, strengths of our study included the large number of patients and that most patients had OSA diagnosed based on PSG.

6. Conclusions

We show that OSA is common in patients in the ICU. Obstructive sleep apnea also appears to be associated with a decreased risk of ICU and hospital mortality. Potential mechanisms may include the protective effects of obesity during critical illness.

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